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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,372	03/04/2002	Eric M. Ferreira	1950-0001	7247

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EXAMINER

NAGUBANDI, LALITHA

ART UNIT PAPER NUMBER

1621

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/091,372		FERREIRA ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Lalitha Nagubandi		1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 December 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-6,8,9,12,13,17-24 and 43-52 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6,8,9,12,13,17-24 and 43-52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                                    |

***Status of the Application***

Claims 1-6,8,9,12,13,17-24 and 43-52 are pending, 1-6,8,9,12,13,17-24 and 45-47 are rejected under 35 U.S.C. 112 first and Second paragraphs. Claims 43,44 and 48-52 are objected to as being dependent upon a rejected claim. Claim 47 is currently amended.

***Response to Arguments***

Applicants' arguments, filed on December 27<sup>th</sup>, 2005, with respect to the previous office action dated June 29<sup>th</sup>2005, have been fully considered and are persuasive. The rejection under 35 U.S.C. 112, first and second paragraphs of claims 1-6,8,9,12,13, 17-24 and 45 has been withdrawn. Further, the rejection of claims 46 and 47, under 35 U.S.C. 112, first paragraph has been withdrawn in view of the applicants arguments.

***Claim Rejections - 35 USC § 112***

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8,9,12,13,17,19, and 21-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "enantioselective oxidation of secondary alcohols", does not reasonably provide enablement for the

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“ enantioselective oxidation of other organic systems by using the same chiral catalyst claimed in the instant application”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the *Wands factors* (MPEP 2164.01 (a)) as the instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApl 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the existence of working examples; and (8) the quantity of experimentation necessary. All of the *Wands factors* have been considered with regard to the instant application, with the most relevant factors discussed below.

#### ***Nature of the Invention***

All of the rejected claims are drawn to an invention which pertains to a method of catalyzing an enantioselective oxidation reaction of an oxidizable chiral organic compound composed of a racemic mixture, comprising the organic compound with an oxidizing agent and a catalyst.

***Breadth of the Claims***

The complex nature of the claims is greatly exacerbated by breadth of the claims. Claims 1-6 and 8,9,12,13,17,19,20, and 43-52 encompass a method of catalyzing an enantioselective oxidation reaction of an organic compound consisting of alcohols, thiols, amines, and phosphines in presence of a catalyst comprising a palladium composition. Moreover, a catalyst comprising of Pd, and a chiral ligand containing two or more tertiary N-atoms separated by two or more linking atoms is rather unclear.

***Guidance of the Specification/ Working Examples***

There is no guidance given by the specification as to what type of chiral catalyst has to be used to achieve the effective enantioselective oxidation in the case of amines, thiols, phosphines etc.

All of the guidance provided by the specification is directed towards enantioselective oxidation of the secondary alcohols such as phenyl ethanol rather than the enantioselective oxidation of the other organic systems claimed in the instant application.

All of the working examples provided by the specification are directed towards the enantioselective oxidation of Secondary alcohols only. Applicants provide in the specification on pages 19-31 (examples 1-3) Pd catalyzed enantioselective oxidation of secondary alcohols using mostly (-) sparteine as the chiral ligand.

***State of the Art***

While the state of the art is relatively high with regard to enantioselective oxidation of secondary alcohols, different organic systems with varied functional groups

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are expected to behave in a different manner; hence the state of the art with regard to the enantioselective oxidation of the organic systems mentioned by the applicants is underdeveloped. In particular, there do not appear to be any examples or teachings in the art wherein the compounds similar to the ones claimed, comprising amines, thiols and phosphines etc., are enantioselectively oxidized by the catalyst described in the present application. Moreover, applicant provides, in the specification on page 8, the broad description of the catalyst and a chiral ligand, specifically used for the enantioselective oxidation of secondary alcohols.

***Predictability of the Art***

The instant application is directed to a method of catalyzing an enantioselective oxidation reaction of an oxidizable, chiral organic compound composed of a racemic mixture, with an oxidizing agent and a catalyst comprising a Pd and a chiral ligand containing two or more tertiary nitrogen atoms separated by two or more linking atoms. Further, the organic compound selected from the group consisting of alcohols, thiols, amines and phosphines is rather broad and unclear.

In the instant case, the instant catalysts are highly unpredictable since one skilled in the art cannot fully describe, visualize or recognize the identity of the genus of the catalyst, by structure, formula or chemical name. Hence, in the absence of fully recognizing the identity of the members of the catalyst and the organic compounds herein, one of skill in the art would be unable to fully predict which catalyst would have the claimed properties described.

*The amount of Experimentation Necessary*

In order to practice claimed invention of one of skilled in the art would have to first envision a combination of appropriate mixture of enantiomers, a suitable catalyst etc. and an appropriate model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for the enantioselective oxidation. If successful, which is unlikely given the lack of significant guidance from the specification, one skilled in the art would have to then either envision a modification of the combination or envision an entirely new combination of the above, and test the desired compound again, whose success is unpredictable. Therefore, it would require undue experimentation to practice the claimed invention to develop enantioselective oxidation of systems ranging from alcohols to phosphines as claimed in the instant application.

Hence, a method of enantioselective oxidation reaction of alcohols, thiols, amines, and phosphines using a catalyst comprising of Palladium composition and a selected enantiomer of chiral ligand containing two or more tertiary nitrogen atoms that are separated by two or more linking atoms, has not been considered enabled by the instant specification.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3,8,18, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Yasuhiro Uozumi et al ( *J.A.C.S.* 1997,119,5063-5064).

The claims are directed to a method of catalyzing an enantioselective Wacker-type cyclization reaction of organic compounds in presence of a catalyst comprising of a palladium composition of a chiral ligand containing two or more tertiary nitrogen atoms that are separated by two or more linking atoms. Further the enantioselective reaction is carried out in presence of an oxidizing agent like benzoquinone.

Uozumi et al disclose Wacker type cyclization of *O* – allylphenols by use of Palladium (II) catalysts coordinated with chiral bis (oxazoline) ligands based on 1,1'-binaphthyl backbone resulting in 97% enantioselectivity. It was found that the combination of palladium bis (trifluoroacetate), (S, S)-2,2'-bis[4-(alkyl) oxazolyl]-1,1'-binaphthyls(S, S) boxax and p-benzoquinone organizes a new efficient catalyst system with much higher enantioselectivity. (See page 5063, column 1, second Para, and Column 2, second para, page 5064, column 1, first para, *J.A.C.S.* 1997,119,5063-5064).



***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 18, and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uozumi et al (*J.Am.Chem.Soc.* 1997,119,5063-5064) and further in view of Hosokawa et al (*J. Am. Chem. Soc.* 1981,103,2318-2323).

Applicants claim a method of catalyzing an enantioselective oxidation reaction of an oxidizable, chiral organic compound composed of a racemic mixture of first and second enantiomers, comprising: contacting an organic compound with an oxidizing agent and a catalyst in presence of an organic solvent. The organic compound is selected from the group consisting of alcohols, thiols, amines and phosphines. The oxidizing agent

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consisting of molecular oxygen, benzoquinone, Cu (I) and (II) salts. Further, the enantioselective oxidation reaction is claimed as an enantioselective Wacker-type cyclization reaction.

***Determination of Scope and content of the Prior Art (MPEP§2141.01)***

Uozumi et al (*J.Am.Chem.Soc.* 1997,119,5063-5064) teach high enantioselectivity, of upto 97% ee in the Wacker-type cyclization of *O*- allyl phenols by use of palladium (II) catalysts coordinated with chiral bis (oxazoline) ligands based on 1,1'-binaphthyl backbone (See page no. 5063).

Hosokawa et al teach (*J. Am. Chem. Soc.* 1981,103,2318-2323) metal catalyzed cyclization of 2-allylphenols leading to optically active 2,3-dihydrobenzofurans. The Wacker-type oxidation catalyzed by chiral Pd (II) complexes in the presence of Cu (II) salts and O<sub>2</sub> is discussed. See pages 2320 and 2321.

***Ascertainment of the difference between the Prior Art and Claims (MPEP § 2141.02)***

The difference between the instant method and Uozumi et al (*J.Am.Chem.Soc.* 1997,119,5063-5064) is that the instant process requires a catalyst comprising of palladium composition, with a chiral ligand containing two or more tertiary nitrogen atoms that are separated by two or more linking atoms, and oxidizing agents like molecular oxygen, benzoquinone, and Cu salts. Further, the enantioselective oxidation being conducted in presence of an organic solvent, whereas Uozumi requires Palladium (II) catalysts coordinated with chiral bis (oxazoline) ligands based on 1,1'- binaphthyl backbone. Uozumi et al do not suggest molecular oxygen for the enantioselective oxidation reaction.

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However, Hosokawa et al (*J. Am. Chem. Soc.* 1981,103,2318-2323) teach the use of Cu salts and molecular oxygen along with the Pd composition for the asymmetric cyclization of 2-allylphenols. Further, Hosokawa et al teach the use of various organic solvents (see Table 1, *J. Am. Chem. Soc.* 1981,103, page 2318).

***Finding of prima facie obviousness – rational and motivation (MPEP § 2142-2143)***

Accordingly, one of ordinary skill in the art would be motivated to prepare the instant products by combining the above references and modify the process of an enantioselective oxidation reaction, because Uozumi taught several Palladium (II) compositions in combination with chiral ligands including compounds involving tertiary nitrogens, as is evident from the Table 1 and also the scheme depicted on page no. 5064, first column (*J. Am. Chem. Soc.* 1997,119,5063-5064). Further, it would have been obvious to one of ordinary skill in the art to try different chiral ligands like (S, S)-Ph-PYBOX, (R)-BINAP, (-)-Cinchonidine, (-) brucine, (DHQ)<sub>2</sub>PHAL and (-) Sparteine etc., so as to obtain higher percentage of enantioselectivity depending on the substrate used. Hence, the use of a suitable Pd composition with an appropriate chiral ligand is obvious to one of ordinary skill in the art and an ordinary artisan would have had a reasonable expectation of success and hence it is a prima facie obvious.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lalitha Nagubandi whose telephone number is 571 272 7996. The examiner can normally be reached on 6.30am to 3.00pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571 272 0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

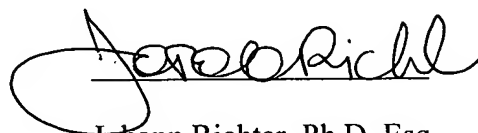
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Lalitha Nagubandi

Patent Examiner

Technology Center 1600

March 20<sup>th</sup>, 2006

A handwritten signature in black ink, appearing to read 'Johann Richter', is written over a horizontal line.

Johann Richter, Ph.D. Esq.

Supervisory Patent Examiner

Technology Center 1600